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Effectiveness of shock and kill strategy for eliminating HIV-1 brain infection: a mathematical modeling study

Antiretroviral therapy (ART) has greatly reduced the overall morbidity and mortality of human immunodeficiency virus-1 (HIV-1) infected patients. Even with the success of ART, the virus persists in many different cells and tissues, and tissues that have minimal ART penetration and limited host immune responses make ideal locations for viral reservoirs. These viral reservoirs contain latently infected long-lived cells. The “Shock and Kill” therapy aims to reactivate latently infected cells by latency reversing agents (LRAs) and kill these reactivated cells by strategies involving the host immune system and certain drugs. The brain is a natural anatomical reservoir for HIV-1 infection. A mathematical model was used to qualitatively analyze the dynamics of latently and productively infected cells in the brain during viral infection and this mathematical model was used to simulate the “Shock and Kill” therapy in the brain. Our model produces the clinical and experimental observation that effective ART can suppress productively infected brain macrophages but leaves a latent reservoir of brain macrophages. By adding a reactivation rate of the latent reservoir into the model, the “Shock and Kill” therapy is analyzed both mathematically and numerically to investigate strategies leading to the eradication of the latent reservoir of brain macrophages.